

### (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

# (19) World Intellectual Property Organization

International Bureau



## . I TERRE BUILDER IN BERNE DER BEIN BERN BERN BERN BERN BERNE HIER HER HILL ERFE HILL ERFE BUILD ER HER LEICHE

(43) International Publication Date 12 February 2004 (12.02.2004)

PCT

## (10) International Publication Number WQ 2004/013130 A1

(51) International Patent Classification<sup>7</sup>: C07D 409/04, 413/04, 409/14, 417/14, 413/14, A61K 31/38, A61P 35/00

(21) International Application Number:

PCT/GB2003/003168

(22) International Filing Date: 24 July 2003 (24.07.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

0218040.4 0310462.7 2 August 2002 (02.08.2002) GB 7 May 2003 (07.05.2003) GB

(71) Applicant (for all designated States except US): AR-GENTA DISCOVERY LIMITED [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19 5TR

(72) Inventors; and

(GB).

(75) Inventors/Applicants (for US only): ARCHER, Janet, Ann [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19,5TR (GB) BORDOGNA, Walter [IT/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19,5TR (GB). BULL, Richard, James [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19,5TR (GB). CLARK, David, Edward [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19,5TR (GB). DYKE, Hazel, Joan [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19, 5TR (GB). GILD, Matthew, Iain, Andrew [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19, 5TR (GB). GILD, Matthew, Iain, Andrew [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19, 5TR (GB). HARRIS, Neil, Victor

[GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19 5 R (GB). VAN DEN HEUVEL, Marco [NL/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19 5 TR (GB); PRICE, Stephen [GB/GB]; 8/9 Spire Green Centre, Flex Meadow, Harlow, Essex CM19 5 TR (GB).

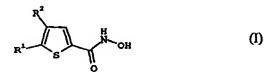
- (74) Agents: COCKERTON, Bruce, Roger et al.; Carpmaels & Ransford, 43 Bloomsbury Square, London WC1A 2RA (GB).
- (81) Designated States (national)! AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SUBSTITUTED THIENYL-HYDROXAMIC ACIDS AS HISTONE DEACETYLASE INHIBITORS



(57) Abstract: A compound of formula (I): which can be used in the treatment of diseases associated with histone deacetylase enzymatic activity.





nal Application No

PCT/GB 03/03168 A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D409/04 C07D413/04 C07D409/14 C07D417/14 C07D413/14 A61K31/38 A61P35/00 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to daim No. JUNG M ET AL: "Analogues of trichostatin Α 1 - 34A and trapoxin B as histone deacetylase inhibitors" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 7, no. 13, 8 July 1997 (1997-07-08), pages 1655-1658, XP004136274 ISSN: 0960-894X the whole document Α WO 02 26696 A (ROMERO MARTIN MARIA ROSARIO 1 - 34;FINN PAUL W (GB); HARRIS C JOHN (GB);)
4 April 2002 (2002-04-04) claim 1; example 189 X Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents : "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. \*O\* document referring to an oral disclosure, use, exhibition or document published prior to the international filing date but later than the priority date daimed "&" document member of the same patent family Date of the actual completion of the International search Date of mailing of the international search report 3 November 2003 17/11/2003 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016

Form PCT/ISA/210 (second sheet) (July 1992)

Fritz, M



Inte al Application No PCT/GB 03/03168

		PCT/GB 03/03168					
C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  Category Citation of document, with indication, where appropriate, of the relevant passages  Relevant to claim No.							
Category	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.				
A	RICHON V M ET AL: "A CLASS OF HYBRID POLAR INDUCERS OF TRANSFORMED CELL DIFFERENTIATION INHIBITS HISTONE DEACETYLASES" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, no. 6, 17 March 1998 (1998-03-17), pages 3003-3007, XP001120542 ISSN: 0027-8424 table 1		1-34				
A	WO 00 66555 A (ZHANG PUWEN; ZHI LIN (US); FENSOME ANDREW (US); JONES TODD K (US);) 9 November 2000 (2000-11-09) Cf. ex. 60 the whole document		1-34				



Intel al Application No PCT/GB 03/03168

Patent de cited in sea		Publication date	Patent family member(s)		Publication date	
WO 022	6696 A	04-04-2002	AU	9013401		08-04-2002
			CA	2423868		04-04-2002
			EP	1335898		20-08-2003
			WO	0226696		04-04-2002
WO 006	6555 A	09-11-2000	US	6355648	3 B1	12-03-2002
			AU	4681400	A	17-11-2000
			BG	106078	3 A	31-05-2002
			BR	0010216	5 A	19-03-2002
			CA	2371633	3 A1	09-11-2000
			CN	1349499	9 T	15-05-2002
			CZ	20013950	0 A3	12-06-2002
			EP	1181279	5 A1	27-02-2002
			HU	0200993	3 A2 .	29-07-2002
			JP	2002543182	2 T	17-12-2002
			NO	20015380	A C	03-01-2002
			PL	351407	7 A1	22-04-2003
			SK	15902001	1 A3	06-11-2002
			TR	200103288		22-04-2002
			MO	006655	5 A1	09-11-2000
			US	2002103248		01-08-2002
			US	2002169198	B A1	14-11-2002
			US	658314		24-06-2003